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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,150	03/26/2002	Terrence R. Burke Jr.	401371	6328
23548	7590	09/13/2004	EXAMINER	
LEYDIG VOIT & MAYER, LTD 700 THIRTEENTH ST. NW SUITE 300 WASHINGTON, DC 20005-3960			LUKTON, DAVID	
			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 09/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/937,150

**Applicant(s)**

BURKE JR. ET AL.

**Examiner**

David Lukton

**Art Unit**

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 June 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 39-49, 67, 68, 73, 78, 85, 86, 91-93, 107, 113, 116-118 and 120-136 is/are pending in the application.
- 4a) Of the above claim(s) 86, 91-93, 107, 113, 118, 125, 131, 132, 134 and 135 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 39-49, 67, 68, 73, 78, 85, 116, 117, 120-124, 126-130, 133, 136 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Pursuant to the directives of the response filed 6/29/04, claims 39, 67, 73, 85, 86, 91-93, 107, 117, 118, 122 and 123 have been amended, claims 1-9, 24, 27, 30, 31, 35, 72, 119 cancelled, and claims 124-136 added. Claims 39-49, 67, 68, 73, 78, 85, 86, 91-93, 107, 113, 116-118, 120-136 are now pending. Claims 39-49, 67, 68, 73, 78, 85, 116, 117, 120-124, 126-130, 133, 136 are examined in this Office action; claims 86, 91-93, 107, 113, 118, 125, 131, 132, 134, 135 are withdrawn from consideration.

Applicants' arguments filed 6/29/04 have been considered and found persuasive in part. The rejection of claim 123 under 35 USC §101 is withdrawn. The rejection of claim 123 under 35 USC §112, first paragraph is also withdrawn.



Claim 39 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1, 10 or 11 of U.S. Patent No. 6,307,090. Although the conflicting claims are not identical, they are not patentably distinct from each other; there is overlap of the claimed genera.

In response, applicants have argued that if one were to look at claim 1 of the patent in a vacuum, without regard to what is in the description, and without regard to what is in any of the dependent claims, one could not be certain that the term "secondary amino group" is such as to include an arylalkylamino group. Whether this particular statement is true or not is of little consequence. The skilled artisan would find no prohibition against reading the description

to determine what the terms mean. And even if the skilled artisan believed that such a prohibition existed, there still remains the matter of claims 10 and 11, which provide explicit structures. Applicants have not attempted to explain how the skilled artisan confronted with the structures of claims 10 and 11 would fail to recognize that compounds falling within the scope of those claims also fall within the scope of instant claim 39.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d)



The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 133 and 136 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 133 is drawn to a method of treating cancer; claim 133 is drawn to a method of enhancing the therapeutic effect of an unspecified drug. As it happens, neither of these

is enabled. As stated on page 27, line 31, the  $IC_{50}$  for MAP kinase inhibition for compound 126 is 12.5 micromolar. It is also asserted (page 28, line 10+) that compound 126 inhibits growth of MDA-MB 453 cells. Also asserted (page 28, line 12+) that compound 126 inhibits growth of MDA-MB 453/M1 breast cancer xenographs. Also asserted (page 44, line 16-17) is that compounds 11, 12 and 20a exhibited  $IC_{50}$  values in the range of 100 – 500 nM using the surface plasmon resonance SH2 domain binding assay described in Yao (*J. Med. Chem.* **42** 25, 1999). On page 44, line 28+, and figure 17b, it is asserted that compound 126 inhibits proliferation of MDA-MB-453 cells. Results of an experiment are also shown in figure 17a. As stated on page 3, line 23, figure 17a shows an experiment undertaken on human breast cancer cells. On page 45, line 20+, it is asserted that compound 11 inhibited production of MAP kinase in MDA-453 cells that had been treated with heregulin. On page 45, line 30+, it is asserted that compound 126 inhibited colony formation of HBC-474 and MDA-453 cell lines. However, no data is reported, and again questions of control experiments and statistical analysis come to the fore.

Thus, what applicants have shown is that one or more compounds within the claimed genus are effective to inhibit MAP kinase, to inhibit binding of an SHC phosphopeptide to a protein containing a Grb2 SH2 domain, and that one or more compounds within the claimed genus can inhibit growth of certain cells. However, no evidence is presented that there exists even one disease which can be successfully treated in a patient by administering one of the claimed compounds.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988), the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. The following references discuss the matter of various attempts by oncologists to treat cancer: Viallet (*Lung Cancer* **15** (3) 367-73, 1996); Kemeny (*Seminars in Oncology* **21** (4 Suppl 7) 67-75, 1994); Newton (*Expert Opinion on Investigational Drugs* **9** (12) 2815-29, 2000); Giese (*Journal of Cancer Research and Clinical Oncology* **127** (4) 217-25, 2001); Garattini (*European Journal of Cancer* **37** Suppl 8 S128-47, 2001); Ragnhammar (*Acta Oncologica* **40** (2-3) 282-308, 2001). As is evident, attempts to treat cancer using agents which have exhibited *in vitro* activity leads to "unpredictable" results.

As mentioned on page 2, line 20+ (specification) and in Yao (*J. Med. Chem.* **42** 25, 1999), proteins containing the Grb2 SH2 domain are linked to signaling events involving RAS proteins. As it happens, attempting to treat cancer using farnesyl protein transferase inhibitors leads to "unpredictable" results:

- Moasser (*Breast Cancer Research and Treatment* **73** (2) 135-44, 2002) discloses (e.g., abstract) that FT inhibitor sensitivity does not correlate with the relative expression of Ras isoforms or the inhibition of Ras processing, growth factor signaling, expression of estrogen receptor or the overexpression of growth factor receptors. Also stated (last paragraph) is that Ras is not a molecular marker to

guide FT inhibition therapy. This reference does not support the proposition that attempts to treat cancer patients will necessarily result in failure. However, it does support the proposition that there may be many forms of cancer which will be resistant to the effects of FT inhibition.

- Jiang (*Molecular and Cellular Biology* **20** (1) 139-48, 2000) discloses that while AKT2-transformed NIH 3T3 cells are sensitive to FTI-277, but that *ras*-transformed NIH 3T3 cells are not. This supports the proposition that one cannot predict which cells will be sensitive to FT inhibitors.
- Prendergast (*Molecular and Cellular Biology* **14** (6) 4193-202, 1994) discloses that the FT inhibitor L-739,749 inhibited growth of *ras*-transformed fibroblasts. However, L-739,749 had no effect on the growth, morphology, or actin organization of *v-raf*-transformed cells. This supports the proposition that one cannot predict which cells will be sensitive to FT inhibitors.
- Njoroge (*J. Med. Chem.* **40** (26) 4290-301, 1997) discloses that the Ras farnesyl-protein transferase inhibitor SCH 44342 did not show appreciable *in vivo* antitumor activity. This supports the proposition that *in vitro* activity is not necessarily predictive of therapeutic efficacy.
- Lerner (*Oncogene* **15** (11) 1283-8, 1997) discloses that the Ftase inhibitor FTI-277 is highly effective at blocking oncogenic H-Ras but not K-Ras4B processing and signaling. The results obtained demonstrate that while FTI-277 inhibits N-Ras and H-Ras processing in the human tumor cell lines evaluated, inhibition of K-Ras processing requires both an FTase inhibitor and a GGTase I inhibitor.
- Whyte (*J Biol Chem* **272**, 14459, 1997) discloses that geranylgeranyl transferase-1 is structurally related to farnesyl transferase, and that geranylgeranyl transferase-1 may alternatively prenyl K-Ras, thereby bypassing the effect of FPTase inhibition.
- Sharma (*Annals of Oncology* **13** (7) 1067-71, 2002) discloses results of a phase II trial of SCH 66336, an FPTase inhibitor, in patients with metastatic colorectal cancer. No objective responses were observed. It is concluded that future development of this compound cannot be recommended as monotherapy in this disease.

Thus, attempts to treat cancer lead, in general, to "unpredictable" results, as do attempts to

treat cancer using Ftsase inhibitors. Accordingly, it stands to reason that in attempting to treat cancer in humans using compounds which inhibit binding of an SHC phosphopeptide to a protein containing a Grb2 SH2 domain, "unpredictable" results will be obtained.

Accordingly, "undue experimentation" would be required to practice the invention of claims 133 and 136.

In response to the foregoing, applicants have argued that the compounds are effective to inhibit MAP kinase. This particular assertion has not been previously (or presently) challenged by the examiner. Applicants have also argued that the examiner has provided no basis to doubt applicants' assertions regarding therapeutic efficacy. However, there are numerous examples in the literature of compounds exhibiting promising effects on cancer cell proliferation *in vitro*, but which compounds turn out not to be effective when administered to humans stricken with cancer, or even to tumor-bearing rats. The fact of this supports the examiners' assertion of "unpredictability". At the same time, there is no evidence of record which shows that inhibitors of erb-2 signalling are effective to treat cancer in humans (or other mammals).

Applicants have also argued that the examiners of US Patents 6,743,786 and 6,740,661 have abstained from imposing an enablement rejection in cases involving treatment of cancer and inhibition of FPTase. Applicants have further argued that because the examiners of USP '786 and '661 have abstained from imposing enablement rejections, it is a violation of patent law for any other examiner to impose an enablement rejection in a case involving



treatment of cancer or FPTase inhibition. However, applicants are not correct. The examiner of one application is not bound by decisions made by other examiners in other patent applications. The validity of a rejection in a given application is determined on the basis of the merits of that rejection. If applicants believe that this ground of rejection is improper, it is suggested that applicants do the following: (a) provide references published before 3/23/99 which show that cancer could be successfully treated in humans (or other mammals) using compounds which inhibit erb-2 signalling, and (b) explain why, in the face of so much "failure" in the treatment of cancer, that the examiner's assertions regarding "unpredictability" are incorrect.

Notwithstanding the foregoing, the possibility of allowing a claim drawn to a method of treating breast cancer in a mammalian patient will be considered.



Claims 39-49, 67, 68, 73, 78, 85, 116, 117, 120-124, 126-130, 133, 136 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 39, it is recited, in reference to "W", that the alkyl and aryl portions of the substituents can be substituted with "keto". However, a "keto" group must be bonded to two groups, not one. Accordingly, the claim is rendered indefinite as to what other substituent can be bonded to the keto group.
- In claim 39, the following is recited (last two lines):

"contains a ...substituent at a position *para*- to the alkylamido group".

Here, the phrase “the alkylamido group” lacks antecedent basis. For example, in claim 120, there are five amide groups. Corresponding to these five amide groups, there are at least seven unique alkylamido groups. Which are intended?

- Claim 121 recites that the carrier is “pharmacologically acceptable”. The term “pharmacology” pertains to the study of drugs. The term “pharmaceutical”, on the other hand, pertains to formulation of drugs. Accordingly, it would seem more appropriate to recite that the carrier is *pharmaceutically acceptable*, than it is to recite that the carrier is “pharmacologically acceptable”.
- Claim 136 is drawn to a “method of enhancing the therapeutic effect of a treatment”. This renders the claim indefinite as to the nature of the treatment, and the objectives of the treatment. One might infer that one of the embodiments encompassed by the claim would be to enhance the antineoplastic efficacy of an anticancer drug which has been administered to a patient who has been stricken with cancer. However, the claim is not limited to this. For example, suppose that a tumor-bearing patient has a headache, and takes aspirin to relieve the headache. Is it applicants’ position that the analgesic effect of the aspirin will be augmented by the claimed compounds? Or suppose that a patient with pancreatic cancer also has high blood pressure. Is it applicants position that the antihypertensive effect of a blood pressure medication will be enhanced? Further, the term “treatment” encompasses actions undertaken by health care professionals in addition to administration of pharmaceutical agents. For example, suppose that a patient with melanoma also has a backache and seeks treatment from a chiropractor. Most of the “treatment” undertaken by chiropractors involves body movements, muscle and ligament stretching and massage. Is it applicants position that the effects of the chiropractor’s actions will be enhanced by the claimed compounds?



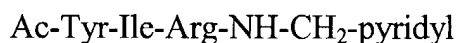
The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39, 40, 49, 72, 78, 85 are rejected under 35 U.S.C. §102(a) as being anticipated by Al-Obeidi (USP 5,849,510).

As indicated previously, Al-Obeidi discloses (col 22, line 15+) the following compound:



This anticipates claim 39 when the substituent variables are as follows:

Y is Phe substituted with hydroxyl

W is alkylcarbonyl

n is 2

Z is heteroarylalkylamino

In response, applicants have argued that the term "arylheterocycle" is such as to mandate the presence of at least two rings, one of which is aromatic (and contains no heteroatoms), and the other of which is heterocyclic. The examiner would agree that this is one possible interpretation of the term at issue. However, another reasonable interpretation is that the

term "aryl" merely qualifies that the heterocyclic group is aromatic. According to this interpretation, one ring would suffice. Applicants may endeavor to amend the claims to eliminate the possibility that the term "aryl" can be an adjective which qualifies the term "heterocycle". Until that time, however, the maintaining of this rejection is justified.



Claims 39, 40, 49, 67, 78 are rejected under 35 U.S.C. §102(e) as being anticipated by Larsen (USP 6,410,585).

Larsen discloses (col 219) a compound designated "example 43". This anticipates claim 39 when the substituent variables are as follows:

W = carboxyalkylcarbonyl

Y = Phe substituted with carboxyalkoxy

n = zero

Z = 3-phenylpropylamino

In response to this ground of rejection, applicants have argued that they have incorporated the limitations of claim 72 into claim 39. However, applicants are not correct. Claim 72, as presented in the amendment filed 2/26/04 required that "Z" be aryl heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkylamino. While claim 39 permits this as an option for "Z", claim 39 does not require it. Accordingly, it is not correct to say that the limitations of claim 72 have been incorporated into claim 39. If applicants believe that this ground of rejection is improper, it is suggested that they provide a detailed explanation as to why this conclusion has been reached. (Better still

would be to amend the claims to overcome the rejection).

The rejection is maintained.



Claims 39, 40, 49, 67, 78 are rejected under 35 U.S.C. §102(e) as being anticipated by Horwell (USP 5,981,755).

Horwell discloses (col 21) the compound of example # 34. This anticipates claim 39 when the substituent variables are as follows:

W = benzyloxycarbonyl

Y = Phe substituted with hydroxyl

n = zero

Z = benzyl

In response to this ground of rejection, applicants have argued that they have incorporated the limitations of claim 72 into claim 39. However, applicants are not correct. Claim 72, as presented in the amendment filed 2/26/04 required that "Z" be aryl heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkylamino. While claim 39 permits this as an option for "Z", claim 39 does not require it. Accordingly, it is not correct to say that the limitations of claim 72 have been incorporated into claim 39.

The rejection is maintained.



Claim 39 is rejected under 35 U.S.C. §102(e) as being anticipated by Burke (USP 6,307,090).

Burke discloses 5 compounds in claim 11 (col 67, line 48+). Each of these anticipates instant claim 39. The compounds in claim 11 are the first, third and fourth ones listed. With regard to the phosphonoalkyl and phosphonohaloalkyl groups, the proviso in the last two lines of claim 39 is noted.

In response to this ground of rejection, applicants have argued that they have incorporated the limitations of claim 72 into claim 39. However, applicants are not correct. Claim 72, as presented in the amendment filed 2/26/04 required that "Z" be aryl heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkylamino. While claim 39 permits this as an option for "Z", claim 39 does not require it. Accordingly, it is not correct to say that the limitations of claim 72 have been incorporated into claim 39.

Applicants have also argued that the proviso in the last three lines of claim 39 is effective to exclude the Burke compounds (USP '090). However, this is not true. First, one could reasonable argue that in none of the compounds in claim 11 of the patent is there a phenylalanyl group in which an alkylamido group is present on the phenyl ring of phenylalanine (whether ortho, meta, or para). Rather, what is present on the phenyl ring is a group which could be named in any of several ways, such as the following:



The point is that an N-oxalylamino alkylamido group is not an alkylamido group *per se*, and so

the proviso in the last three lines of claim 39 does not apply at all. Furthermore, even if it were true that an N-oxalylamino alkylamido group is equivalent to an alkylamido group (which is certainly not the case), it would still remain true that at least two of the compounds in claim 11 (USP '090) do not meet the limitation of having the *ortho* and *meta* positions unsubstituted.

The rejection is maintained.



Claim 39 is rejected under 35 U.S.C. §102(e) as being anticipated by Hiyoshi (USP 5,824,862).

Hiyoshi discloses (col 53) SEQ ID NO: 13 which has the following sequence:

G-Y-R-G-F-Y

This peptide anticipates the claims when applicants' substituent variables correspond as follows:

W = methylcarbonyl which is substituted with amino

Y = phenylalanine which is substituted with hydroxyl

AA<sup>1</sup> = arginine

AA<sup>2</sup> = glycine

AA<sup>3</sup> = phenylalanine

n = 3

Z = phenethylamino which is substituted with carboxyl and with hydroxyl.

In response to this ground of rejection, applicants have argued that they have incorporated the limitations of claim 72 into claim 39. However, applicants are not correct. Claim 72, as presented in the amendment filed 2/26/04 required that "Z" be aryl heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkylamino. While claim 39 permits this as an option for "Z", claim 39 does not require it. Accordingly, it is not correct to say that the limitations of claim 72 have been incorporated into claim 39.

The rejection is maintained.



Claim 39 is rejected under 35 U.S.C. §102(e) as being anticipated by Harding (USP 6,022,696)

Harding discloses (col 59) SEQ ID No: 1, and (col 69) SEQ ID No: 14. These are, respectively, the following:

VYIHPF

KYIHPF

The first of these is encompassed by claim 39 when the substituent variables correspond as follows:

W = alkylcarbonyl which is substituted with amino

Y = phenylalanine which is substituted with hydroxyl

AA<sup>1</sup> = Ile



$AA^2 = \text{His}$

$AA^3 = \text{Pro}$

$n = 3$

$Z = \text{phenethylamino}$  which is substituted with carboxyl

In response to this ground of rejection, applicants have argued that they have incorporated the limitations of claim 72 into claim 39. However, applicants are not correct. Claim 72, as presented in the amendment filed 2/26/04 required that "Z" be aryl heterocyclyl  $C_1-C_6$  alkylamino. While claim 39 permits this as an option for "Z", claim 39 does not require it. Accordingly, it is not correct to say that the limitations of claim 72 have been incorporated into claim 39.

The rejection is maintained.



Claim 39 is rejected under 35 U.S.C. §102(e) as being anticipated by Landry (USP 5,948,658).

Landry discloses (col 67) SEQ ID NO: 76 which has the following sequence:

D-Y-N-M-Y

This peptide anticipates the claims when applicants' substituent variables correspond as follows:

$W = \text{2-methylpropionyl}$  which is substituted with amino and with carboxyl

Y = phenylalanine which is substituted with hydroxyl

AA<sup>1</sup> = Asn

AA<sup>2</sup> = Met

n = 2

Z = phenethylamino which is substituted with carboxyl and with hydroxyl.

In response to this ground of rejection, applicants have argued that they have incorporated the limitations of claim 72 into claim 39. However, applicants are not correct. Claim 72, as presented in the amendment filed 2/26/04 required that "Z" be aryl heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkylamino. While claim 39 permits this as an option for "Z", claim 39 does not require it. Accordingly, it is not correct to say that the limitations of claim 72 have been incorporated into claim 39.

The rejection is maintained.



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No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

*D. Lukton*  
DAVID LUKTON  
PATENT EXAMINER  
GROUP 1809